

REMARKS

In response to the Final Office Action dated March 4, 2011, Applicants provide the following remarks that are made without prejudice to the prosecution of any subject matter in a related divisional, continuation or continuation-in-part application. Claims 1-30 are pending. Claims 4, 13, 15 and 16 have been amended. Claims 1-3, 5-12, 14 and 17-30 have been withdrawn from consideration.

Claims 4, 13, 15 and 16 have each been amended to recite an embodiment wherein the metal is in solution. Claims 4, 15 and 16 have been further amended to clarify that the mass spectrometric analysis is performed on a solution comprising the metal-organic residue complex bound to the sugar chain or the sugar chain-containing substance. The above amendments are fully supported by the specification as filed. For example, the paragraph bridging pages 30-31 describes analysis of the recited solutions, and Example 9 describes preparation of the same. Accordingly, no new matter has been added by way of this amendment.

Rejection under 35 U.S.C. § 103

Claims 4 and 13 stand rejected under 35 U.S.C § 103 as being unpatentable over U.S. Patent Application Pub. No. 2005/0074551 (“Huang”) in view of PCT Pub. No. WO 98/59362 (“Hutchens”), and claims 15 and 16 stand rejected under 35 U.S.C § 103 as being unpatentable over Hutchens in view of U.S. Patent No. 4,511,658 (“Lambert”). In short, the Examiner is of the opinion that it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the teachings of the above disclosures to arrive at the claimed invention. Applicants respectfully disagree.

Claims 4, 13, 15 and 16 each recite a metal-organic residue complex, wherein the metal is in solution and comprises a surface which enables diffuse reflection of a laser beam. Claims 4, 15 and 16 are directed to methods for mass spectrometric analysis of a solution comprising the metal-organic residue complex bound to a sugar chain or sugar chain-containing substance. Claim 13 is directed to a method for trapping a sugar chain or a sugar chain-containing substance with the metal-organic residue complex. Such trapping methods are useful,

for example, for mass spectrometric analysis of the sugar chain or sugar chain-containing substance.

The recited methods may be used for accurate and sensitive real-time monitoring of enzymatic reactions related to sugar chains. In this regard, Applicants have discovered that employing a metal-organic residue complex comprising a metal in solution provides the unexpected benefit of being able to use the reaction solution directly for mass spectrometric analysis without further processing (specification at page 30, line 26 to page 31, line 9). In addition, since the metal comprises a surface which enables diffuse reflection of a laser beam, such analyses can be performed even in the presence of high concentrations of buffers or salts (see *e.g.*, specification at page 30, line 26 to page 31, line 8 and Example 18). Accordingly, the claimed subject matter advantageously provides for direct observation and kinetic analysis of enzymatic reactions in a reaction solution. These aspects of the claimed subject matter are not suggested, much less taught, by the cited art.

Huang is directed to the fabrication of nanodevices comprising biological molecules (*e.g.*, proteins and nucleic acids) attached to nanoparticles (Huang at paragraph [0045]). Huang discloses that proteins attached to nanoparticles (*e.g.*, metals) can be analyzed by gel electrophoresis and ion exchange chromatography (Huang Examples 6 and 7). However, in no instance does Huang teach or suggest mass spectrometric analysis of a solution comprising a sugar chain or sugar chain-containing substance bound to a metal-organic residue complex. Nor does Huang disclose, or even suggest, that the disclosed nanoparticles comprise a metal comprising a surface which enables a diffuse reflection of a laser beam or that use of the same would provide the noted benefits. Accordingly, this reference provides absolutely no motivation to arrive at the instantly claimed subject matter.

Hutchens does not cure the deficiencies of Huang. Hutchens discloses retentate chromatography methods comprising chip arrays. Hutchens notes that analytes (*e.g.*, proteins) can be separated based on their ability to adsorb to an adsorbent (Hutchens at page 4, lines 6-8), and these adsorbants can be attached to a substrate (*e.g.*, a metal) in an array of pre-determined, addressable locations (Hutchens at page 4, lines 31-32 and page 7, lines 17-20). Substrates disclosed by Hutchens include strips, plates and substrates removably insertable into a detector

(Hutchens at page 27, lines 18-23 and page 28, lines 29-30). In no instance does this reference teach or suggest mass spectrometric analysis of a solution comprising a sugar chain or sugar chain-containing substance bound to a metal-organic residue complex as recited in the instant claims. Furthermore, this reference lacks any teaching or suggestion of the properties or associated benefits of the recited metal-organic residue complex. Accordingly, this reference also fails to provide any motivation to arrive at the claimed subject matter.

Although not specifically taught in either reference, the Examiner believes that both Huang and Hutchens disclose a metal organic residue complex which inherently comprises a metal surface which enables a diffuse reflection of a laser beam. In response, Applicants note that “[o]bviousness cannot be predicated on what is not known at the time an invention is made, even if the inherency of a certain feature is later established.” MPEP 2141.02 (subsection V) citing *In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993). Accordingly, even assuming *arguendo* that Huang and Hutchens inherently disclose a metal organic residue complex comprising a metal surface which enables a diffuse reflection of a laser beam as the Examiner believes, these references cannot render the instant claims obvious since the inherent properties (and corresponding benefits) of the recited metal-organic residue complex are not taught by these references, and were not known at the time of filing of the instant application.

Lambert is directed to a colorimetric analysis for formaldehyde comprising the use of a 4-amino-3-hydrazino-5-mercapto-1,2,4-triazole (AHMT) ketone amination (Lambert at column 1, lines 46-66). Lambert does not provide any teaching or suggestion to use AHMT, or any other organic residue, in a mass spectrometric analysis of a solution comprising a sugar chain or sugar chain-containing substance bound to a metal-organic residue complex.

In summary, the cited references, either alone or in any combination, clearly do not teach or suggest the claimed subject matter. Huang is directed to electrophoresis and ion chromatography methods and provides no motivation to modify the array-based method of Hutchens to arrive at the recited solution-based mass spectrometry methods. Even assuming that Huang and Hutchens inherently disclose a metal organic residue complex having the recited properties, these references cannot render the instant claims obvious since such properties, and

the noted advantages, were not known at the time of filing and were not taught by either Huang or Hutchens. Finally, Lambert simply notes that formaldehyde may be detected based on a color change upon reaction with AHMT, and both Hutchens and Lambert are devoid of any motivation to combine such formaldehyde detection methods with Hutchens' disclosure to arrive at the claimed subject matter. Accordingly, Applicants submit that the pending claims are patentable over the cited references (*i.e.*, nonobvious) and request that this ground of rejection be withdrawn.

The Director is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

All of the claims remaining in the application are now clearly allowable.
Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,
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